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7 April 2005

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(54) Title: STAPHYLOCOCCUS AUREUS EFB PROTEIN AND C3 BINDING REGION WHICH INHIBIT COMPLEMENT ACTIVATION

(57) Abstract: The Efb protein from *Staphylococcus aureus* has now been shown to have the ability to bind to the C3 protein which is a crucial component in the activation of complement, and a specific C3 binding region has been located at the C-terminal end of the Efb protein. Isolated proteins and protein fragments containing the Efb protein C3 binding region are thus provided which have complement inhibiting activity, and these proteins and fragments are particularly useful in therapeutic methods wherein the inhibition of complement is desirable, such as in the treatment of hemolytic anemia, the prevention of graft or implant rejection, and to alleviate complement activation that is associated with kidney dialysis methods such as hemodialysis.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/11949

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C07K 1/00, 2/00; A61K 39/02, 39/085, 39/38, 39/00
US CL : 530/350, 300, 825; 524/234.1, 243.1, 185.1, 184.1, 190.1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 530/350, 300, 825; 524/234.1, 243.1, 185.1, 184.1, 190.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BODEN M.K. et al. Cloning and characterization of a gene for a 19 kDa fibrinogen-binding protein from Staphylococcus aureus. Mol. Microbiol. 1994, Vol. 12, No. 4, pages 599-606, especially page 602 and Figure 6.	1-5, 9, 14, 15 and 20
X	US 2002/0173462 A (BODEN et al) 21 November 2002 (21.11.2002), see line 5 of Figure 11.	1-5, 9, 14, 15 and 20
Y	BODEN M.K. et al. Evidence for three different fibrinogen-binding proteins with unique properties from Staphylococcus aureus strain Newman. Microb. Pathogenesis, 1992, Vol. 12, pages 289-298, entire document.	1-5, 9, 14, 15 and 20
Y	BODEN K.B. et al. Fibrinogen-binding protein/clumping factor from Staphylococcus aureus. Infect. Immun. August 1989, Vol. 57, No. 8, pages 2358-2363, see entire document.	1-5, 9, 14, 15 and 20
X	US 6,299,879 B (BODEN et al.) 09 October 2001 (09.10.2001), see line 5 of Figure 6.	1-5, 9, 14, 15 and 20

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 December 2004 (30.12.2004)	09 FEB 2005
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer S. Devi, Ph.D. Telephone No. (703) 308-0196 DEBORAH A. THOMAS PARALEGAL SPECIALIST GROUP 1800

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/11949

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-5, 9, 14, 15, and 20 (in part)

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/11949

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-5, 9, 14, 15 and 20 (in part), drawn to an isolated C3 binding region from the *S. aureus* Efb protein having the ability to inhibit complement activation, and a composition, vaccine and a kit comprising the same.

Group II, claims 6-8, 10 and 11, drawn to an isolated antibody that recognizes the C3 binding region from the *S. aureus* Efb protein, and a composition and a kit comprising the same; and a method of diagnosing an *S. aureus* infection using the antibody.

Group III, claims 12, 16-19, 21 and 22 (in part), and 25-27, drawn to a method of inducing an immunological response and a method of inhibiting complement activity by administering an isolated C3 binding region from the *S. aureus* Efb protein.

Group IV, claim 13, drawn an isolated nucleic acid coding for the C3 binding region from the *S. aureus* Efb protein.

Group V, claim 20 (in part), drawn to a composition comprising the *S. aureus* Efb protein.

Group VI, claims 18, 19, 21 and 22 (in part), and 25-27, drawn to a method of inhibiting complement activation and a method of treating haemolytic anemia by administering the *S. aureus* Efb protein.

Group VII, claim 23, drawn to a method of reducing the induction of complement activation by a prosthetic tissue or organ transplant by coating the implant with an Efb protein or the C3 binding region of the same.

Group VIII, claim 24, drawn to a method of inducing an immunological response by administering the C3 binding region of the *Staphylococcus epidermidis* Efb protein.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical features of inventions I-VIII are delineated above. The special technical features of inventions I, II, IV and V are a C3 binding region from the *S. aureus* Efb protein, an antibody that recognizes the same, an isolated nucleic acid coding for the C3 binding region, and a composition comprising the *S. aureus* Efb protein, respectively. These special technical features do not share a significant common structure and immunogenic or biologic functions. Furthermore, Boden *et al.* (*Mol. Microbiol.* 12: 599-606, 1994) has already taught the C-terminal half of the 19 kDa recombinant Fib protein of *S. aureus,* i.e., the C3 binding region from the *S. aureus* Efb protein. Invention III is drawn to the first method of using the product of invention I. Although the product of invention I and the first method of using or making the same is a permitted combination under PCT Rule 13.2, in the instant case, since the product is already taught in the art, the special technical feature does not define over the prior art. Technically, the absence of special technical feature permits the separation of the method of using the product from the product itself. Invention VI is

drawn to a method of using the product of invention V. However, a composition comprising the *S. aureus* Efb protein is disclosed by Boden *et al.* (*Mol. Microbiol.* 12: 599-606, 1994), and therefore is not a special technical feature. The methods of inventions III, VI, VII and VIII do not share a common method step and/or a composition or a reagent.

Continuation of B. FIELDS SEARCHED Item 3:
DIALOG, WEST, MEDLINE, EMBASE, BIOSIS
(Efb or Fib or SAC3 or 19 kDa), aureus, C3 or complement bind? or activat?; inventors' names